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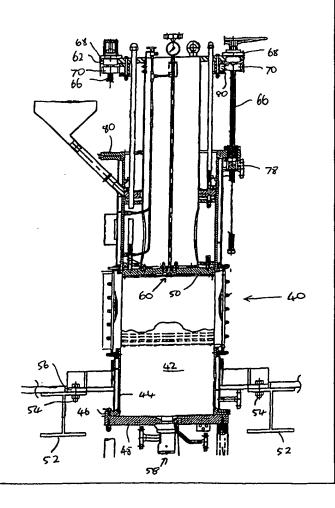
#### **Published**

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#### (54) Title: CHROMATOGRAPHIC COLUMN

#### (57) Abstract

A chromatography column (40) in which an adjustable cell assembly (50) is movable within a housing (44) by a support assembly including three ball-threaded rods (66) interlinking the adjustable cell assembly (50) and housing (44). Each rod (66) is rotatable but longitudinally fixed in a base plate (64) fixed to the adjustable cell assembly (50). A ball nut (78) is mounted on each rod (66) and fixed to a flange (60) fixed to the housing (44). Fixed to each rod (64) is a spur gear (70), all the gears (70) being interconnected by a ring gear (80). A handwheel fixed to one rod (66) allows manual adjustment of all the rods (66) simultaneously to provide rapid adjustment of the position of the adjustable cell assembly (50) relative to the housing (44).



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### CHROMATOGRAPHY COLUMN

The present invention relates to a chromatography column.

Frequently it is desirable to separate out one or more useful components from a fluid mixture that contains other components which may not be useful or are less valuable. To accomplish this it is often necessary or desirable to fractionate such a fluid mixture to separate out the useful or desired components. This can be carried out by using liquid chromatography systems. Liquid chromatography may briefly be described as the fractionation of components of a mixture based on differences in the physical or chemical characteristics of the components. The various liquid chromatographic systems fractionate the components with a fractionation matrix. Some liquid chromatographic matrix systems fractionate the components of a mixture based upon such physical parameters as molecular weight. Still other chromatographic systems will fractionate components of a mixture based upon such chemical criteria as ionic charge, hydrophobicity, and the presence of certain chemical moieties such as antigenic determinants or lectin-binding sites on the components.

Chromatography systems of various sized are used in both laboratory analysis operations and for industrial

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scale production operations in which separation steps such as separating out a fraction from human blood or separating out impurities from a pharmaceutical can be carried out on a large scale in a batch process.

A typical known construction of chromatography column is shown in Figure 1 in which a column tube 2 for holding a chromatography medium is defined laterally by a cylindrical housing 4, a fixed cell assembly 6 fixed at one end of the cylindrical housing 4 (in this case the lower end of the housing 4) and an adjustable cell assembly 8 towards the other end of the housing 4 (in this case the upper end of the housing 4). Upper and lower valve assembly 10 and 12 provide access to the column tube 2 from outside the column tube 2.

The adjustable cell assembly 6 is relatively movable within, and sealable to, the cylindrical housing 4. It is held in place beneath a support plate 14 by a number of threaded rods 16, which plate 14 is in turn, supported by a flange 18 on the housing 4 by a number of rods 20 between the plate 14 and flange 18. Each rod 18 is fixed to the support plate 14 but passes through a respective throughhole in the flange 18 and fixed relative to it by a pair of bolts 22,24 mounted on each rod above and below the flange 18.

Adjustments of the position of the adjustable cell

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assembly 6 within the housing 4 is a very time consuming process. If the adjustable cell assembly 8 is to be moved upwards, the nut 22 of one rod must be loosened, by a quarter turn say, and the nut 24 moved upwards by that amount. This is repeated until all the nut positions on the rods 20 have been adjusted by the same small amount. The sequence is then repeated, possibly many times, until the adjustable cell assembly 8 is in the desired new position.

Similarly if the adjustable cell assembly is to be forced downwards, to compact a chromatography medium in the column tube for example, the lower nut 24 on rod is loosened by a quarter turn and upper nut 22 tightened downwards to force the adjustable cell assembly downwards. When all the nuts 22, 24 on the rods 20 have been so adjusted the sequence is repeated until the adjustable cell assembly 6 exerts the required pressure on the chromatography medium.

The adjustment of the position of such adjustable cell assemblies is very time consuming, especially with large industrial columns, and the resultant down-time results is lost productivity as the column is idle while it is being adjusted.

The present invention, which is as claimed in the claims, provides a chromatography column which is more

readily adjustable than such prior art chromatography columns.

An embodiment of the present invention will now be described, by way of example only, with reference to the accompanying drawings, of which:

Figure 1 is a side sectional view of a prior art chromatography column;

Figure 2 is a side sectional view of a chromatography column according to the present invention;

Figure 3 is a detailed side sectional view of a part of the chromatography column of Figure 2; and

Figure 4 is an end view of Figure 3 viewed in the direction IV of Figure 3.

Referring to Figure 2, a chromatography column 40 includes a column tube 42 partially defined by a cylindrical housing 44 with an outwardly extending flange 46 at its lower end to which is bolted, in sealing relationship, a fixed cell assembly 48. The upper end of the column tube 42 is defined by an adjustable cell assembly 50 mounted for movement relative to the housing 44.

The housing 44 is, in this case, mounted on a pair of I-beams 52 by bolts 54 joining the I-beams to an annular collar 56 fixed to surrounding the housing 44.

Access to the interior of the column tube is provided

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by upper and lower valve assemblies 60 and 58. The specific arrangements of these valve assemblies and associated controls are not part of the present invention. They may be any suitable system for the processes to be carried out by the chromatography column 40 and so will not be described in any further detail.

Referring now also to Figures 3 and 4, the housing 44 has at its upper extremity an outwardly extending annular flange 60. The adjustable cell assembly 50 is secured to an annular plate 62. The flange 60 and plate 62 have a series of three, circumferentially spaced apart aligned bores, such as 64, for receiving a respective threaded support rod 66 (one of which is fully shown in Figures 2 and 3).

Each rod 64 is rotatable but fixed longitudinally with respect to the plate 62 by a flange mounted bearing 68 and a keyed spur gear 70. A handwheel 72 is fixed to the upper end of one rod 66 so the rod 66 can be rotated manually.

Each rod 66 is located in a bore 64 of the flange 60 by a retaining housing 74 secured to the flange 60 by a clamp nut 76. A ball nut assembly 78 is located on each rod 66 above the retaining housing 74 and secured to the housing 44 as shown in Figure 2.

An annular ring gear 80 is mounted for rotation on the base plate 62 within a two-part annular mounting 82

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comprising a lower ring with an L-shaped cross-section 84 and an annular top-plate 86.

The ring 84 and top-plate 86 are secured together to hold the ring gear 80 in place, and to the base plate 62, by a number of bolts 88. The ring gear 80 engages each of the spur gars 70 keyed to respective rods 66 which rods 66 are therefore all constrained to rotate together and so be simultaneously adjusted on manual rotation of the handwheel 72. A non-rotatable locking cog (not shown) is movable into and onto of engagement with one of the spur gears 70 locks one rod 66 against rotation, and so all of the rods 66, when the adjustable cell assembly 50 has been moved to the desired position within the housing 44.

The rods 66 may be sufficiently long to allow the adjustable cell assembly 50 to be fully retracted from within the portion of the housing 44 used to define the column tube 42 to allow full access to the interior of the housing 44 by an operator.

The diameter of the handwheel 72 is chosen to allow manual application of the maximum pressure to be applied to compress the chromatography column medium to the required degree.

The support assembly of the embodiment of Figures 2 to 4 provides a compact and efficient means of providing simultaneous adjustment of the adjustable supports (rods

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66) mounting the adjustable cell assembly 50 to the housing 44 but other designs of support assemblies may be employed to put the present invention into effect. The drive means for adjusting the adjustable supports may be an electric motor, for example, which would allow a degree of automation to the adjustment of the position of the adjustable cell assembly 50.

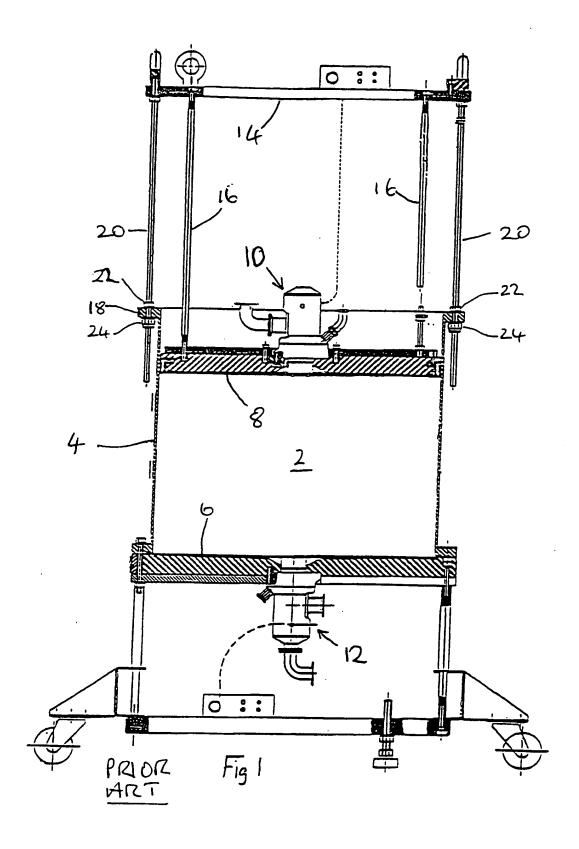
### CLAIMS:

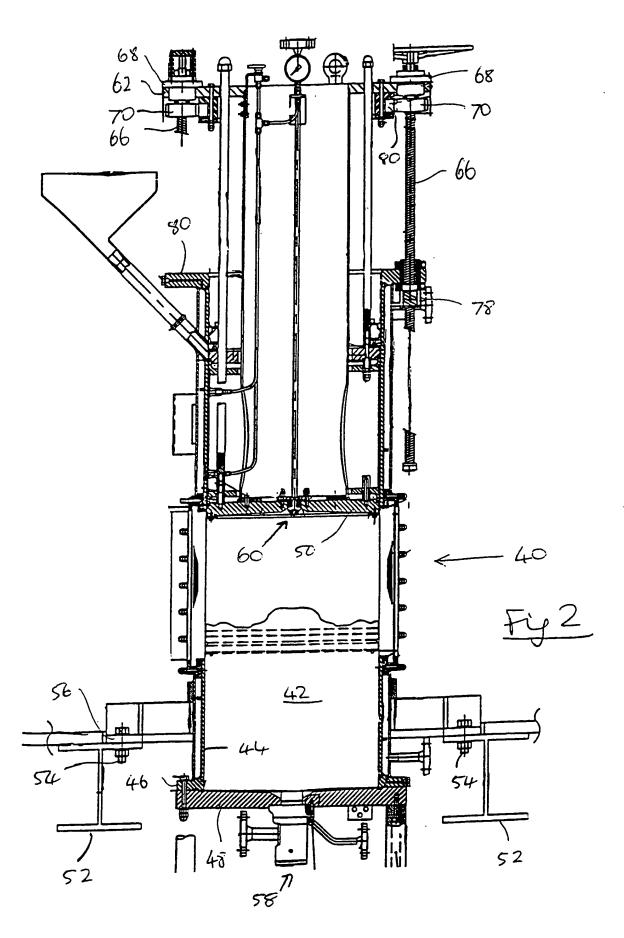
- 1. A chromatography column including a column tube for holding a chromatography medium defined in part by a housing and an adjustable cell assembly movable relative to and within the housing, the adjustable cell assembly being mounted on the housing and movable relative to it by a support assembly which includes a plurality of adjustable supports, the adjustable supports being interconnected such that they are adjustable simultaneously and a drive means for effecting the simultaneous adjustment of the adjustable supports.
- 2. A chromatography column as claimed in claim 1 in which each adjustable support comprises a ball screw assembly which includes a rotatable, ball-threaded rod which is longitudinally fixed to a support on which the adjustable cell assembly is mounted and a ball nut mounted on the rod and secured to the housing.
- 3. A chromatography column as claimed in claim 2 in which each rod has fixed to it a gear wheel, the gear wheels of all the rods being interconnected by a ring gear.
- 4. A chromatography column as claimed in claim 3 in which

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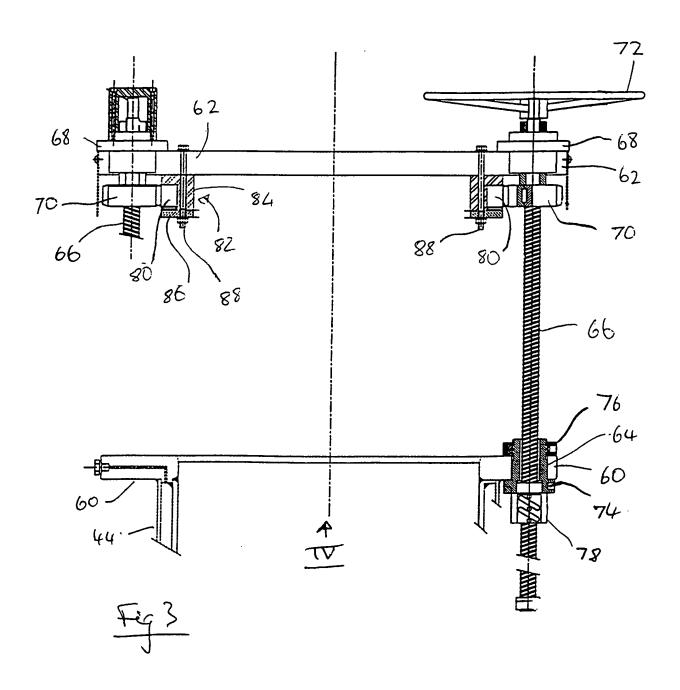
the gear wheels are disposed at the outside of the ring gear.

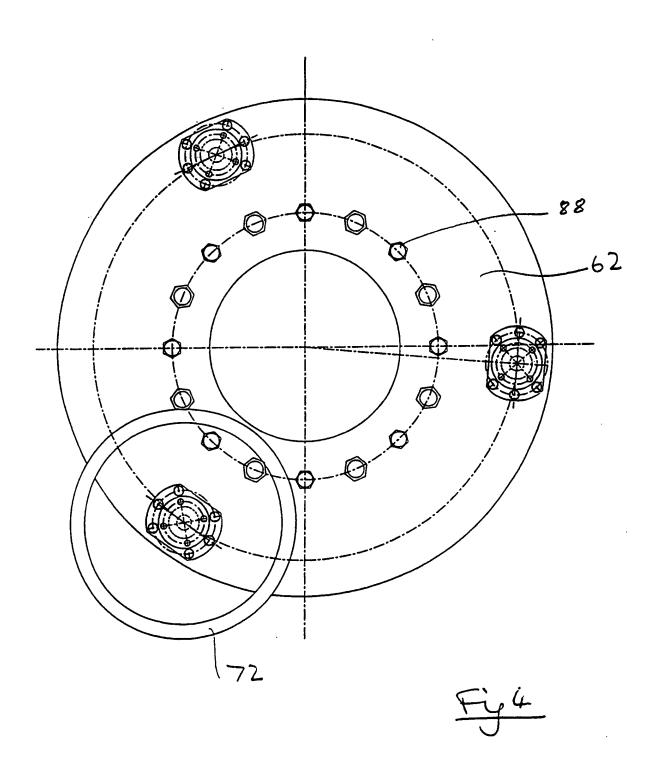
- 5. A chromatography column as claimed in any one of claims 2 to 4 including a handwheel fixed to a rod.
- 6. A chromatography column as claimed in any preceding claim including a brake for releasably holding the support assembly against adjustment by the drive means.
- 7. A chromatography column as claimed in claim 7 as dependent on any claim 3 in which the brake is a non-rotatable gear wheel movable into and out of engagement with a gear wheel of one of the rods.
- 8. A chromatography column having a support assembly substantially as hereinbefore described, or as shown in, Figures 2 to 4 of the accompanying drawings.





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# INTERNATIONAL SEARCH REPORT

Inter .onal Application No PCT/GB 99/01284

A. CLASSIF IPC 7	FICATION OF SUBJECT MATTER 801D15/08 G01N30/60			
According to	International Patent Classification (IPC) or to both national classificat	ion and IPC		
B. FIELDS				
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Documentati	ion searched other than minimum documentation to the extent that su	ch documents are included in the fields searched		
Electronic da	ata base consulted during the International search (name of data base	e and, where practical, search terms used)		
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the rele	vant passages F	Relevant to claim No.	
Α	US 4 797 209 A (D.H.A. JACKSON) 10 January 1989 (1989-01-10) column 4, line 31 - line 37; fig	ł	,2,8	
A	EP 0 008 921 A (WRIGHT SCIENTIFIC 19 March 1980 (1980-03-19)	LIMITED)		
Α	US 5 324 426 A (T. JOSEPH) 28 June 1994 (1994-06-28) 		!	
A	US 5 213 683 A (W.H.MANN) 25 May 1993 (1993-05-25)			
Funt	her documents are listed in the continuation of box C.	X Patent family members are listed in annex	τ	
"A" docume consic "E" earlier filling c "L" docume which citatio "O" docum other "P" docum	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another in or other special reason (as specified) sent referring to an oral disclosure, use, exhibition or means ent published prior to the international filling date but	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.		
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter \_onal Application No PCT/GB 99/01284

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4797209	Α	10-01-1989	JP 1199156 A	10-08-1989
EP 8921	Α	19-03-1980	AU 5038379 A JP 55039094 A	13-03-1980 18-03-1980
US 5324426	Α	28-06-1994	NONE	
US 5213683	Α	25-05-1993	FR 2680115 A GB 2258415 A,B US 5282973 A	12-02-1993 10-02-1993 01-02-1994